

AMENDMENTS TO THE CLAIMS

Please amend claims 4, 5, 14, and 29-32 as shown below in the Listing of Claims.

Please cancel claims 1 and 9 without prejudice to or disclaimer of the subject matter therein.

The listing of claims will replace all prior listings of claims in the application.

Listing of Claims

1. (Canceled).
2. (Canceled)
3. (Canceled)
4. (Currently amended) The method of claims 54, wherein prostate cancer, prostate carcinoma or prostate neoplasm is detected or distinguished.
5. (Currently amended) A method for detecting and/or distinguishing between or among prostate cell proliferative disorders in a subject, comprising:
 - [-] a) obtaining, ~~from a subject,~~ a biological sample having subject comprising genomic DNA from a subject;
 - [-] b) contacting the genomic DNA, or a fragment thereof, with at least one reagent or a plurality of reagents for distinguishing between methylated and non methylated CpG dinucleotide sequences within at least one target sequence of the genomic DNA, or fragment thereof, wherein the target sequence comprises, or hybridizes under stringent conditions to, at least 16 contiguous nucleotides of SEQ ID NO: 36, said contiguous nucleotides comprising at least one CpG dinucleotide sequence; and wherein the at least one reagent comprises a single stranded nucleic acid molecule or peptide nucleic acid at least 9 nucleotides in length that hybridizes under stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 130, 131, 248, 249 and

complements thereof.

[-] e) determining, based at least in part on said distinguishing, the methylation state of at least one target CpG dinucleotide sequence, or an average, or a value reflecting an average methylation state of a plurality of target CpG dinucleotide sequences, whereby detecting, or detecting and distinguishing between or among prostate cell proliferative disorders is, at least in part, afforded.

6. (Original) The method of claim 5, wherein distinguishing between methylated and non methylated CpG dinucleotide sequences within the target sequence comprises converting unmethylated cytosine bases within the target sequence to uracil or to another base that is detectably dissimilar to cytosine in terms of hybridization properties.
7. (Previously presented) The method of claim 5, wherein distinguishing between methylated and non methylated CpG dinucleotide sequences within the target sequence(s) comprises methylation state-dependent conversion or non-conversion of at least one CpG dinucleotide sequence to the corresponding converted or non-converted dinucleotide sequence within a sequence selected from the group consisting of SEQ ID NO: 130, 131, 248, 249 and contiguous regions thereof corresponding to the target sequence.
8. (Original) The method of claim 5, wherein the biological sample is selected from the group consisting of cell lines, histological slides, biopsies, paraffin-embedded tissue, bodily fluids, ejaculate, urine, blood, and combinations thereof.
9. (Canceled)
10. (Original) The method of claim 9, wherein the contiguous sequence comprises at least one CpG, TpG or CpA dinucleotide sequence.
11. (Withdrawn) The method of claim 9, comprising use of at least two such nucleic acid molecules, or peptide nucleic acid (PNA) molecules.

12. (Withdrawn) The method of claim 9, comprising use of at least two such nucleic acid molecules, or peptide nucleic acid (PNA) molecules as primer oligonucleotides for the amplification of a sequences selected from the group consisting of SEQ ID NO: 1043, 1044, 172, 173, 98, 99, 130, 131, 1172, 1173, 160, 161, 120, 121, 106, 107, 80, 81, 1051, 1052, 66, 67, 1117, 118, 1045, 1046, 1035, 1036, 94, 95, 1033, 1034, 1049, 1050 , sequences complementary thereto, and regions thereof that comprise, or hybridize under stringent conditions to the primers.

13. (Withdrawn) The method of claim 9, comprising use of at least four such nucleic acid molecules, or peptide nucleic acid (PNA) molecules.

14. (Currently amended) A method for detecting, or detecting and distinguishing between or among prostate cell proliferative disorders in a subject, comprising:

- a. obtaining, from a subject, a biological sample having subject genomic DNA;
- b. extracting or otherwise isolating the genomic DNA;
- c. treating the genomic DNA of b), or a fragment thereof, with one or more reagents to convert cytosine bases that are unmethylated in the 5-position thereof to uracil or to another base that is detectably dissimilar to cytosine in terms of hybridization properties;
- d. contacting the treated genomic DNA, or the treated fragment thereof, with an amplification enzyme and at least two primers wherein each primer comprises a single stranded nucleic acid at least 9 nucleotides in length that hybridizes under stringent conditions to ~~comprising, in each case a contiguous sequence of at least 9 nucleotides that is complementary to, or hybridizes under moderately stringent or stringent conditions to~~ a sequence selected from the group consisting of SEQ ID NO: 130, 131, 248, 249 and complements thereof, wherein the treated genomic DNA or the fragment thereof is either amplified to produce at least one amplicate, or is not amplified; and

- e. determining, based on a presence or absence of, or on a property of said amplificate, the methylation state of at least one CpG dinucleotide of a sequence according to SEQ ID NO: 36, or an average, or a value reflecting an average methylation state of a plurality of CpG dinucleotides of a sequence according to SEQ ID NO: 36, whereby at least one of detecting, or detecting and distinguishing between prostate cell proliferative disorders is, at least in part, afforded.
15. (Original) The method of claim 14, wherein treating the genomic DNA, or the fragment thereof in c), comprises use of a reagent selected from the group consisting of bisulfite, hydrogen sulfite, disulfite, and combinations thereof.
16. (Original) The method of claim 14, wherein contacting or amplifying in d) comprises use of at least one method selected from the group consisting of: use of a heat-resistant DNA polymerase as the amplification enzyme; use of a polymerase lacking 5'-3' exonuclease activity; use of a polymerase chain reaction (PCR); generation of a amplificate nucleic acid molecule carrying a detectable labels; and combinations thereof.
17. (Original) The method of claim 16, wherein the detectable amplificate label is selected from the label group consisting of: fluorescent labels; radionuclides or radiolabels; amplificate mass labels detectable in a mass spectrometer; detachable amplificate fragment mass labels detectable in a mass spectrometer; amplificate, and detachable amplificate fragment mass labels having a single-positive or single-negative net charge detectable in a mass spectrometer; and combinations thereof.
18. (Original) The method of claim 14, wherein the biological sample obtained from the subject is selected from the group consisting of cell lines, histological slides, biopsies, paraffin-embedded tissue, bodily fluids, ejaculate, urine, blood, and combinations thereof.

19. (Withdrawn) The method of claim 14, further comprising in step d) the use of at least one nucleic acid molecule or peptide nucleic acid molecule comprising in each case a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 1043,1044,172,173, 98, 99,130, 131,1172, 1173,160,161,120,121,106,107, 80, 81, 1051,1052, 66, 67,1117, 118,1045,1046,1035, 1036, 94, 95,1033,1034, 1049,1050, and complements thereof, wherein said nucleic acid molecule or peptide nucleic acid molecule suppresses amplification of the nucleic acid to which it is hybridized.
20. (Withdrawn) The method of claim 19, wherein said nucleic acid molecule or peptide nucleic acid molecule is in each case modified at the 5'-end thereof to preclude degradation by an enzyme having 5'-3' exonuclease activity.
21. (Withdrawn) The method of claim 19, wherein said nucleic acid molecule or peptide nucleic acid molecule is in each case lacking a 3' hydroxyl group.
22. (Withdrawn) The method of claim 19, wherein the amplification enzyme is a polymerase lacking 5'-3' exonuclease activity.
23. (Withdrawn) The method of claim 14, wherein determining in e) comprises hybridization of at least one nucleic acid molecule or peptide nucleic acid molecule in each case comprising a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 1043, 1044,172,173, 98,99, 130,131,1172, 1173, 160, 161, 120,121,106, 107, 80, 81,1051,1052, 66, 67,1117,118,1045,1046, 1035, 1036,94, 95,1033,1034,1049, 1050, and complements thereof.
24. (Withdrawn) The method of claim 23, wherein at least one such hybridizing nucleic acid molecule or peptide nucleic acid molecule is bound to a solid phase.

25. (Withdrawn) The method of claim 24, wherein a plurality of such hybridizing nucleic acid molecules or peptide nucleic acid molecules are bound to a solid phase in the form of a nucleic acid or peptide nucleic acid array selected from the array group consisting of linear or substantially so, hexagonal or substantially so, rectangular or substantially so, and combinations thereof.
26. (Withdrawn) The method of claim 24, further comprising extending at least one such hybridized nucleic acid molecule by at least one nucleotide base.
27. (Original) The method of claim 14, wherein determining in e), comprises sequencing of the amplificate.
28. (Original) The method of claim 14, wherein contacting or amplifying in d), comprises use of methylation-specific primers.
29. (Currently amended) The method of claim 14 comprising in d) using primer oligonucleotides comprising one or more CpG; TpG or CpA dinucleotides; and further comprising in e) the use of at least one method selected from the group consisting of: hybridizing in at least one nucleic acid molecule or peptide nucleic acid molecule comprising a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under ~~moderately stringent~~ or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 130, 131, 248, 249, and complements thereof; hybridizing at least one nucleic acid molecule that is bound to a solid phase and comprises a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under ~~moderately stringent~~ or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 130, 131, 248, 249, and complements thereof; hybridizing at least one nucleic acid molecule comprising a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under ~~moderately stringent~~ or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 130, 131, 248, 249, and complements thereof, and extending at least one such

hybridized nucleic acid molecule by at least one nucleotide base; and sequencing in e) of the amplificate.

30. (Currently amended) The method of claim 14 comprising in d) use of at least one nucleic acid molecule or peptide nucleic acid molecule comprising in each case a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under ~~moderately-stringent~~ or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 130, 131, 248, 249, and complements thereof, wherein said nucleic acid molecule or peptide nucleic acid molecule suppresses amplification of the nucleic acid to which it is hybridized; and further comprising in e) the use of at least one method selected from the group consisting of: hybridizing in at least one nucleic acid molecule or peptide nucleic acid molecule comprising a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under ~~moderately-stringent~~ or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 130, 131, 248, 249, and complements thereof; hybridizing at least one nucleic acid molecule that is bound to a solid phase and comprises a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under ~~moderately-stringent~~ or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 130, 131, 248, 249, and complements thereof; hybridizing at least one nucleic acid molecule comprising a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under ~~moderately-stringent~~ or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 130, 131, 248, 249, and complements thereof, and extending at least one such hybridized nucleic acid molecule by at least one nucleotide base; and sequencing in e) of the amplificate.
31. (Currently amended) The method of claim 14, comprising in d) amplification by primer oligonucleotides comprising one or more CpG; TpG or CpA dinucleotides and further comprising in e) hybridizing at least one detectably labeled nucleic acid molecule comprising a contiguous sequence at least 9 nucleotides in length that is complementary

to, or hybridizes under ~~moderately stringent~~ or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 130, 131, 248, 249.

32. (Currently amended) The method of claim 14, comprising in d) the use of at least one nucleic acid molecule or peptide nucleic acid molecule comprising in each case a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under ~~moderately stringent~~ or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 130, 131, 248, 249, and complements thereof, wherein said nucleic acid molecule or peptide nucleic acid molecule suppresses amplification of the nucleic acid to which it is hybridized, and further comprising in e) hybridizing at least one detectably labeled nucleic acid molecule comprising a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under ~~moderately stringent~~ or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 130, 131, 248, 249.

33. (Previously presented) A method for detecting and/or distinguishing between or among prostate cell proliferative disorders in a subject, comprising:

- a. obtaining, from a subject, a biological sample having subject genomic DNA;
- b. extracting, or otherwise isolating the genomic DNA;
- c. contacting the genomic DNA of b), or a fragment thereof, comprising at least 16 contiguous nucleotides of a sequence according to SEQ ID NO: 36, and sequences that hybridize under stringent conditions thereto, with one or more methylation-sensitive restriction enzymes, wherein the genomic DNA is, with respect to each cleavage recognition motif thereof, either cleaved thereby to produce cleavage fragments, or not cleaved thereby; and
- d. determining, based on a presence or absence of, or on property of at least one such cleavage fragment, the methylation state of at least one CpG dinucleotide of a sequence according to SEQ ID NO: 36, or an average, or a value reflecting an

average methylation state of a plurality of CpG dinucleotides of a sequence according to SEQ ID NO: 36, whereby at least one of detecting, or of detecting and differentiating between or among prostate cell proliferative disorders is, at least in part, afforded.

34. (Original) The method of claim 33, further comprising, prior to determining in d), amplifying of the digested or undigested genomic DNA.
35. (Original) The method of claim 34, wherein amplifying comprises use of at least one method selected from the group consisting of: use of a heat resistant DNA polymerase as an amplification enzyme; use of a polymerase lacking 5'-3' exonuclease activity; use of a polymerase chain reaction (PCR); generation of an amplificate nucleic acid carrying a detectable label; and combinations thereof.
36. (Original) The method of claim 35, wherein the detectable amplificate label is selected from the label group consisting of: fluorescent labels; radionuclides or radiolabels; amplificate mass labels detectable in a mass spectrometer; detachable amplificate fragment mass labels detectable in a mass spectrometer; amplificate, and detachable amplificate fragment mass labels having a single-positive or single-negative net charge detectable in a mass spectrometer; and combinations thereof.
37. (Original) The method of claim 33, wherein the biological sample obtained from the subject is selected from the group consisting of cell lines, histological slides, biopsies, paraffin-embedded tissue, bodily fluids, ejaculate, urine, blood, and combinations thereof.
38. (Withdrawn) A treated nucleic acid derived from SEQ ID NO: 1 TO SEQ ID NO: 59, SEQ ID NO: 1017 TO SEQ ID NO: 1028, SEQ ID NO: 1116 AND SEQ ID NO: 1171, wherein the treatment is suitable to convert at least one unmethylated cytosine base of the

genomic DNA sequence to uracil or another base that is detectably dissimilar to cytosine in terms of hybridization

39. (Withdrawn) A nucleic acid, comprising at least 16 contiguous nucleotides of a treated genomic DNA sequence selected from the group consisting of SEQ ID NOs: 60-295, 1029-1076, 1117 — 1120, 1172 — 1175 and sequences complementary thereto, wherein the treatment is suitable to convert at least one unmethylated cytosine base of the genomic DNA sequence to uracil or another base that is detectably dissimilar to cytosine in terms of hybridization.
40. (Withdrawn) The nucleic acid of claims 39 and 44 wherein the contiguous base sequence comprises at least one CpG, TpG or CpA dinucleotide sequence.
41. (Withdrawn) The nucleic acid of claims 39 and 44 wherein the treatment comprises use of a reagent selected from the group consisting of bisulfite, hydrogen sulfite, disulfite, and combinations thereof.
42. (Withdrawn) An oligomer, comprising a sequence of at least 9 contiguous nucleotides that is complementary to, or hybridizes under moderately stringent or stringent conditions to a treated genomic DNA sequence selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 59, SEQ ID NO: 1017 to SEQ ID NO: 1028, SEQ ID NO: 1 to SEQ ID NO: 59, SEQ ID NO: 1017 to SEQ ID NO: 1028, SEQ ID NO: 1116 and SEQ ID NO: 1171.
43. (Withdrawn) The oligomer of claim 42, comprising at least one CpG, CpA or TpG dinucleotide.

44. (Withdrawn) A set of oligomers, comprising at least two oligonucleotides according, in each case, to any one of Claims 42 or 43.

45. (Withdrawn) A kit useful for detecting, or for detecting distinguishing between or among prostate cell proliferative disorders of a subject, comprising:

at least one of a bisulfite reagent, or a methylation-sensitive restriction enzyme; and at least one nucleic acid molecule or peptide nucleic acid molecule comprising, in each case a contiguous sequence at least 9 nucleotides that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NOs: 60- 295,1029-1076,1117 - 1120,1172 -1175 and complements thereof.

46. (Withdrawn) The kit of claim 45, further comprising standard reagents for performing a methylation assay selected from the group consisting of MS-SNuPE, MSP, MethyLight, HeavyMethyl, nucleic acid sequencing, and combinations thereof.

47. (Withdrawn) Use of a method according to claims 1 to 37, a nucleic acid according to claims 38 through 41, an oligomer according to any one of claims 42 and 43, a set of oligonucleotides according to claim 44, and a kit according to claims 45 and 46 for the detection of and/or differentiation between or among prostate cell proliferative disorders.